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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re PATENT APPLICATION of:

LEE

Appln. No. 08/966,223

Group Art Unit: 1645

Filed: November 7, 1997

Examiner: M.P. Allen

FOR: GDF-1

\* \* \*

RULE 132 DECLARATION

I, Ted Ebendal, declare and state as follows:

(1) I reside at Börjegatan 45 B, S-752 29 Uppsala, Sweden.

(2) I am a Professor and Chairman in the Department of Developmental Biology, Faculty of Medicine, Uppsala University since 1988. I hold a Ph.D. (Doctor of Philosophy) degree which was earned from Uppsala University, Sweden in 1976. A copy of my *curriculum vitae* is attached.

(3) I am an author of over 100 peer-reviewed publications in the field of neuronal growth factors and neurotrophic factors.

(4) Recombinant human GDF-1 (rhGDF-1) was provided by Michael Jarpe of Cambridge NeuroScience for use in the assays reported herein.

(5) On information and belief, rhGDF-1 was produced as follows. The cDNA of human GDF-1 (amino acid residues 255 to 373) was cloned into pRSET (Invitrogen). The construct was designed to produce a fusion protein which adds 34 amino acid residues to the N-terminus of rhDGF-1 including six histidine residues. There is an enterokinase cleavage site between the N-terminal extension and the rhGDF-1 sequence to facilitate removal of the tag. However, this extension was not removed for the assays reported herein.

(6) On information and belief, the above-described expression construct was inserted into the *E. coli* cell line BL21(DE3)pLysS to induce rhGDF-1 expression. Expression was induced by the addition of IPTG and was allowed to proceed for 4 hours. rhGDF-1 was produced in inclusion bodies.

(7) On information and belief, the inclusion bodies containing rhGDF-1 were solubilized and folded in 6 M guanidine and 100 mM dithiothreitol. Reducing agent and denaturing agent was removed by reverse phase HPLC. The protein was dried down in a Speed Vac and resuspended in 8 M urea at 5 mg/ml protein concentration. The protein solution was then diluted 1/100 to a final concentration of 50 µg/ml in refolding buffer of 10 mM reduced glutathione, 1 mM oxidized glutathione, and 50 mM Tris buffer (pH 9.0). The rhGDF-1 protein was allowed to refold for 20 hours at 25°C.

(8) On information and belief, a sample of the refolded rhGDF-1 protein was then analyzed by reducing and non-reducing SDS-PAGE. The gel was stained with Coomassie and the proportion of dimer was determined by densitometry. The rhGDF-1 dimer was found to be approximately 20% of total protein. The rhGDF-1 preparation was stored at -80°C.

(9) The following assays were performed under my direction and the results were analyzed by me.

(10) The sample was assayed in a fibre outgrowth assay using sympathetic ganglia from embryonic day 9 chicken embryo explanted into a collagen gel. See Ebendal et al., Journal of Neuroscience Research, vol. 40, pp. 276-284 for a description of the use of explanted ganglia in collagen gels. Neurotrophin-3 (NT-3) only weakly stimulates sympathetic fibre outgrowth in this assay (see panel d of Fig. 4 in Ernfors et al., Proceedings of the National Academy of Science, U.S.A., vol. 87, pp. 5454-5458). Members of the TGF-beta superfamily of proteins potentiate the effects of NT-3 in this assay.

(11) The sample of GDF-1 was diluted 100-fold and then further diluted in culture medium with 1% fetal calf serum as a carrier. GDF-1 was assayed on sympathetic ganglia at a

concentration of 2.5 to 250 ng/ml. The ganglia were examined after two days of incubation using darkfield microscopy. No fibre outgrowth was evoked by GDF-1 at any of these concentrations.

(12) Therefore, the potentiating effect of GDF-1 on neurotrophin activity could be assessed by comparing fibre outgrowth induced by NT-3 in the presence or the absence of GDF-1. Any increased fibre outgrowth caused by the combination of NT-3 and GDF-1 would be due to potentiation, instead of the effects of GDF-1 alone.

(13) The potentiating effect of GDF-1 in the sympathetic fibre outgrowth assay (Ernfors et al., *id.*) was determined with human NT-3 (Austral Biologicals) at a concentration of 2 ng/ml and GDF-1 at concentrations between 0 to 250 ng/ml. Fibre outgrowth density was scored in a blinded fashion by two independent observers with culture dishes arranged in random order. Scores were recorded on a scale from 0 (no fibres) to 5 (very high density of fibres forming a circular halo around the explanted nervous tissue). The assay was repeated three times. The results below represent the mean of the scores given for each culture by each observer.

	GDF-1 concentration	Mean Score
) Medium Only	0 ng/ml	0.0
NT-3 alone	0 ng/ml	1.7
GDF-1 alone	250 ng/ml	0.0
NT-3 + GDF-1	250 ng/ml	3.1
NT-3 + GDF-1	50 ng/ml	2.3
NT-3 + GDF-1	5 ng/ml	1.8

(14) The combination of GDF-1 at 250 ng/ml with NT-3 shows a significant potentiation effect in comparison to the response obtained with NT-3 alone (statistically significant difference at  $P < 0.001$  using Mann-Whitney U test). There is also a clear trend of potentiation of NT-3 by GDF-1 at 50 ng/ml, although this difference is not statistically significant in the present format of the assay.

(15) The specific activity of GDF-1 in the assay shows a reasonable dose-response relationship between 50 to 250 ng/ml.

(16) In view of the above results, I conclude that GDF-1 has biological activity on neurons similar to members of the TGF-beta superfamily of proteins.

(17) I declare further that all statements made herein of my own knowledge are true and that all statements made on

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information and belief are believed true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

x Ted Ebendal  
Ted Ebendal

x April 9, 1998  
Date

## CURRICULUM VITAE for TED EBENDAL

Born: September 21, 1948. Stockholm, Sweden  
Sex: Male  
Marital status: Married, 1 child (born 1974)  
Address: Börjegatan 45 B, S-752 29 UPPSALA, Sweden

### *Education/academic degrees:*

1971 Bachelor of Science. Uppsala University, Sweden  
1972 Master of Science, Uppsala University  
1976 Doctor of Philosophy, Uppsala University  
1977 Docent in Zoology, Uppsala University  
1987 Professor, Faculty of Medicine, Uppsala University

### *Professional Experience:*

1972-76 Teaching Instructor in Zoology, Uppsala University  
1977 Assistant Professor in Zoology, Uppsala University  
1977 Visiting scientist at Strangeways Research Laboratory, Cambridge, England  
1977-81 Docent (Associate Professor) appointment in Zoology, Uppsala University  
1981-87 Research Associate Professor in Neurobiology at the Swedish Natural Science Research Council  
1988- Full Professor of Developmental Biology, Faculty of Medicine, Uppsala University

*Scientific Awards:* King Oscar Prize, Uppsala University (1982). Erik K. Fernström's prize to especially promising young scientists (1991).

*Invited Oral Presentations* have been given at about 80 international meetings.

*Current research interests:* Molecular and developmental neuroscience, development and repair mechanisms in the nervous system, neuronal growth factors and their receptors including NGF, NT-3, GDNF and BMPs. Homologous recombination in transgenic mice using embryonic stem cells.

*Administrative and scientific duties* at the Faculty of Medicine, Uppsala University  
Chairman at the Dept of Developmental Biology (1988-). Member of the Medical Faculty Board (1988-93). Member of various scientific priority committees etc (1988-), Vice Chairman of Neuroscience Center at Uppsala University, (1989-1995).  
Chairman Uppsala University Animal Research Board (1997-)

*Pre-doctoral advisor:* Supervised 11 PhD students of which 8 have finished their PhD thesis and three are on the way.

*Post-doctoral advisor for:* Wilma Friedman (USA, 1986-88), Reg Williams (Australia, 1991-94).

*Organization of scientific meetings, courses* etc: Organized EMBO and BMC Summer School courses for graduate students in Uppsala and at the Karolinska Institute and participated in the organization committees for international meetings in Sweden and abroad (ISDN Biennial Meeting in Tampere 1996, 5th NGF Meeting 1998).

*Referee assignments* etc: Exp. Cell Res., Exp. Brain Res.

*Associate editor:* J. Neurosci. Res., Int. J. Dev. Neurosci, Neuron, Alzheimer's Disease.

*Reviewer of applications* for grants and research positions: Uppsala University, Karolinska Institute, Stockholm University, Umeå University. MRC Sweden, NSF USA and various Swedish Universities.

*Member of scientific committees:* The Swedish Foundation for Brain Research (1995-), The International Human Frontier Science Program (Brain Functions 1996-), The Royal Swedish Academy of Sciences National Committee on Biology (1997-).

*Major funding* (Principal Investigator): Swedish NFR (SEK 900,000/yr for 1997 to 1999).

*Publications:* Over 300 scientific papers, reviews and reports in the area of developmental neuroscience



# SELECTED LIST OF PAPERS PUBLISHED BY TED EBENDAL

- 1 Ebendal, T. & Hedlund, K.-O. 1974. Histology of the chick embryo trigeminal ganglion and initial effects of its cultivation with and without nerve growth factor. *Zoon* 2: 25-35.
- 3 Ebendal, T. 1974. Scanning electron microscopy of the chick embryo nerve fibres and heart fibroblasts on collagen substrata *in vitro*. *Zoon* 2: 99-104.
- 4 Ebendal, T. & Hedlund, K.-O. 1975. Effects on nerve growth factor on the chick embryo trigeminal ganglion in culture. *Zoon* 3: 33-47.
- 5 Ebendal, T. 1975. Effects of nerve growth factor on the synthesis of nucleic acids and proteins in cultured chick embryo trigeminal ganglia. *Zoon* 3: 159-167.
- 6 Ebendal, T. & Jacobson, C.-O. Human glial cells stimulating outgrowth of axons in cultured chick embryo ganglia. *Zoon* 3: 169-172.
- 7 Ebendal, T. 1976. The relative roles of contact inhibition and contact guidance in orientation of axons extending on aligned collagen fibrils *in vitro*. *Exp. Cell Res.* 98: 159-169.
- 12 Ebendal, T. 1977. Extracellular matrix fibrils and cell contacts in the chick embryo: Possible roles in orientation of cell migration and axon extension. *Cell Tissue Res.* 175: 439-458.
- 13 Ebendal, T. 1976. Migratory mesoblast cells in the young chick embryo examined by scanning electron microscopy. *Zoon* 4: 101-108.
- 14 Ebendal, T. & Jacobson, C.-O. 1977. Tissue explants affecting extension and orientation of axons in cultured chick embryo ganglia. *Exp. Cell Res.* 105: 379-387.
- 16 Ebendal, T. & Jacobson, C.-O. 1977. Tests of possible role of NGF in neurite outgrowth stimulation by glial cells and heart explants in culture. *Brain Res.* 131: 373-378.
- 17 Ebendal, T. 1977. A cover glass dish for cell cultures intended for observation with inverted microscopes. *Zoon* 5: 73-75.
- 18 Ebendal, T. & Heath, J.P. 1977. Self-contact inhibition of movement in cultured chick heart fibroblasts. *Exp. Cell Res.* 110: 469-473.
- 19 Schultzberg, M., Ebendal, T., Hökfelt, T., Nilsson & Pfenninger, K. 1978. Substance P-like immunoreactivity in cultured spinal ganglia from chick embryos. *J. Neurocytol.* 7: 107-117.
- 20 Dunn, G. A. & Ebendal, T. 1978. Contact guidance on oriented collagen gels. *Exp. Cell Res.* 111: 475-479.
- 22 Dunn, G. A. & Ebendal, T. 1978. Some aspects on contact guidance. In: *Formshaping Movements in Neurogenesis* (ed. C.-O. Jacobson and T.Ebendal), *Zoon* 6: 217-223. Almqvist & Wiksell International, Stockholm.
- 23 Hedlund, K.-O. & Ebendal, T. 1978. Different ganglia from the chick embryo in

- studies on neuron development in culture. In: Formshaping Movements in Neurogenesis (ed. C.-O. Jacobson and T. Ebendal), Zoon 6: 217-223. Almqvist & Wiksell International, Stockholm.
- 24 Ebendal, T., Jordell-Kylberg, A. & Söderström, S. 1978. Stimulation by tissue explants on nerve fibre outgrowth in culture. In: Formshaping Movements in Neurogenesis (ed. C.-O. Jacobson and T. Ebendal), Zoon 6: 235-243. Almqvist & Wiksell International, Stockholm.
- 27 Ebendal, T. 1979. Stage-dependent stimulation of neurite outgrowth exerted by nerve growth factor and chick heart in cultured embryonic ganglia. *Dev. Biol.* 72: 276-290.
- 28 Ebendal, T., Belew, M., Jacobson, C.-O. & Porath, J. 1979. Neurite outgrowth elicited by embryonic chick heart: partial purification of the active factor. *Neurosci. Lett.* 14: 91-95.
- 29 Olson, L., Ebendal, T. & Seiger, Å. 1979. NGF and anti-NGF: Evidence against effects on fiber growth in locus coeruleus from cultures of perinatal CNS tissues. *Dev. Neurosci.* 2: 160-176.
- 32 Löfberg, J. & Ebendal, T. 1979. Substrate topography and shape of motile cells. *Experientia* 36: 508-510.
- 33 Olson, L., Seiger, Å., Ebendal, T. & Hoffer, B. 1980. Comparisons of nerve fiber growth from three major catecholamine producing cell systems: adrenal medulla, superior cervical ganglion and locus coeruleus. In: *Histochemistry and Cell Biology of Autonomic Neurons, SIF cells and Paraneurons* (ed. O. Eränkő et al.), pp. 27-34. Raven Press, N.Y.
- 34 Jacobson, C.-O., Ebendal, T., Hedlund, K.-O. & Norrgren, G. 1981. Factors stimulating neurite outgrowth in chick embryo ganglia. In: *Control Mechanisms in Animal Cells - Specific Growth Factors* (ed. L. Jimenez de Azua et al.), pp. 325-332. Raven Press, N.Y.
- 35 Hedlund, K.-O. & Ebendal, T. 1980. The chick embryo nodose ganglion: effects of nerve growth factor in culture. *J. Neurocytol.* 9: 665-682.
- 36 Ebendal, T., Olson, L., Seiger, Å. & Hedlund, K.-O. 1980. Nerve growth factors in the rat iris. *Nature (London)* 286: 25-28.
- 37 Norrgren, G., Ebendal, T., Belew, M., Jacobson, C.-O. & Porath, J. 1980. Release of nerve growth factor by human glial cells in culture. *Exp. Cell Res.* 130: 31-39.
- 41 Ebendal, T. 1981. Control of neurite extension by embryonic heart explants. *J. Embryol. Exp. Morphol.* 61: 289-301.
- 42 Ebendal, T. 1982. Orientational behaviour of extending neurites. In: *Cell Behaviour* (ed. R. Bellairs, A.S.G. Curtis & G. Dunn) pp. 281-297. Cambridge University Press.
- 44 Olson, L., Björklund, H., Ebendal, T., Hedlund, K.-O. & Hoffer, B. 1981. Factors regulating growth of catecholamine-containing nerves, as revealed by transplantation experiments. *Ciba Found. Symp.* 83: 213-231.
- 49 Richardson, P.M. & Ebendal, T. 1982. Nerve growth activities in rat peripheral

nerve. Brain Res. 246: 57-64.

- 50 Carri, N.G. & Ebendal, T. 1983. Organotypic cultures of neural retina: neurite outgrowth stimulated by brain extracts. Dev. Brain Res. 6: 219-229.
- 52 Ebendal, T., Hedlund, K.-O., & Norrgren, G. 1982. Nerve growth factors in chick tissues. J. Neurosci. Res. 8: 153-164.
- 53 Ebendal, T., Norrgren, G. & Hedlund, K.-O. 1983. Nerve growth-promoting activity in the chick embryo: Quantitative aspects. Med. Biol. 61: 65-72.
- 56 Ebendal, T. 1984. Nerve growth-promoting activities in embryonic and adult tissues. In: Organizing Principles of Neural Development (ed. S.C. Sharma), pp. 93-107, NATO ASI Series A: Vol. 78, Plenum Press, N. Y.
- 57 Norrgren, G., Ebendal, T., Gebb, C. & Wikström, H. 1984. The use of Cytodex 3 microcarriers and reduced-serum media for the production of nerve growth promoters from chicken heart cells. Devel. Biol. Stand. 55: 43-51.
- 58 Ebendal, T., Norrgren, G., Carri, N.G. & Belew, M. 1985. Nerve growth factors in peripheral tissues and CNS. In: Upper Motor Neuron Functions and Dysfunctions, Recent Achievements in Restorative Neurology. Vol. I (ed. Sir John Eccles & M.R. Dimitrijevic), pp. 311-320. Karger, Basel.
- 59 Ebendal, T., Olson, L., Seiger, Å. & Belew, M. 1984. Nerve growth factors in chick and rat tissues. In: Cellular and Molecular Biology of Neuronal Development (ed. I. B. Black) pp. 231-242. Plenum Press, New York.
- 60 Ebendal, T., Olson, L. & Seiger, Å. 1983. The level of nerve growth factor (NGF) as a function of innervation: A correlative radioimmunoassay and bioassay study of the rat iris. Exp. Cell Res. 148: 311-317.
- 70 Norrgren, G., Wikström, H. & Ebendal, T. 1984. Production of nerve growth promoting factor(s) from chick embryo heart cells. Use of Cytodex 3 microcarriers and serum-free media. Exp. Cell Res. 152: 427-435.
- 71 Ayer-LeLièvre, C.S., Ebendal, T., Olson, L. & Seiger, Å. 1983. Localization of nerve growth factor-like immunoreactivity in rat nervous tissue. Med. Biol. 61: 296-304.
- 73 Olson, L., Ebendal, T. & Seiger, Å. 1984. Intraocular grafting of cultured brain tissue: Growth, vascularization and neuron survival in locus coeruleus and cortex cerebri. Neurosci. Lett. 47: 139-144.
- 74 Ebendal, T. & Lundin, L.-G. 1984. Nerve growth factor in three neurologically deficient mouse mutants (*Swl*, *Sp* and *dt<sup>J</sup>*). Neurosci. Lett. 50: 121-126.
- 75 Richardson, P.M., Ebendal, T. & Riopelle, R. 1985. Nerve growth and nerve growth factor within peripheral nervous tissue. In: Neural Grafting in the Mammalian CNS (ed. A. Björklund and U. Stenevi), pp. 319-327. Elsevier.
- 76 Olson, L., Strömberg, I. Herrera-Marschitz, Ungerstedt, U. & Ebendal, T. 1985. Adrenal medullary tissue grafted to the dopamine-denervated rat striatum: Histochemical and functional effects of additions of nerve growth factor. In: Neural Grafting in the Mammalian CNS. (ed. A. Björklund and U. Stenevi), pp. 505-518. Elsevier.

- 78 Ebendal, T., Lärkfors, L., Ayer-LeLievre, C., Seiger, Å. & Olson, L. 1985. New approaches to detect NGF-like activity in tissues. In: *Hormones and Cell Regulation*, Vol. 9 (ed. J.E. Dumont, B. Hamprecht & J. Nunez), pp. 361-376. Elsevier, Amsterdam.
- 79 Strömberg, I., Ebendal, T., Seiger, Å. & Olson, L. 1985. Nerve fiber production by intraocular adrenal medullary grafts: Stimulation by nerve growth factor or sympathetic denervation of the host iris. *Cell Tissue Res.* 241: 241-249.
- 80 Strömberg, I., Herrera-Marschitz, M., Ungerstedt, U., Ebendal, T. & Olson, L. 1985. Chronic implants of chromaffin tissue into the dopamine-denervated striatum. Effects of NGF on survival, fiber growth and rotational behavior. *Exp. Brain Res.* 60: 335-349.
- 82 Norrgren, G. & Ebendal, T. 1986. Nerve growth factor in medium conditioned by embryonic chicken heart cells. *Int. J. Devl. Neurosci.* 4: 41-49.
- 95 Carri, N.G. & Ebendal, T. 1986. Selected optic lobe extracts stimulating retinal neurite outgrowth. In: *Progress in Developmental Biology*, part A (ed. H.C. Slavkin). Alan R. Liss, Inc., N.Y., pp. 119-122.
- 96 Belew, M. & Ebendal, T. 1986. Chick embryo nerve growth factor. Fractionation and biological activity. *Exp. Cell Res.* 167: 550-558.
- 97 Carri, N.G. & Ebendal, T. 1986. A method for explantation of selected areas of the neural retina. *Anat. Rec.* 214: 226-229.
- 98 Whittemore, S.R., Ebendal, T., Lärkfors, L., Seiger, Å., Strömberg, I. & Persson, H. 1986. Developmental and regional expression of  $\beta$  nerve growth factor messenger RNA and protein in the rat central nervous system. *Proc. Natl. Acad. Sci. USA* 83: 817-821.
- 99 Thompson, W.J., Bicker, G., Changeux, J.-P., Ebendal, T.L., Heisenberg, M., Henderson, C.E., Huttner, W., Kandel, E.R., Mallet, J.B., Stent, G.S., Thoenen, H. & Yaniv, M. 1987. Activity-dependent regulation of gene expression (Group report). In: *The Neural and Molecular Bases of Learning* (ed. J.-P. Changeux & M. Konishi). Dahlem Workshop Reports, Life Sciences 38: 13-29. John Wiley, Chichester.
- 100 Whittemore, S.R., Lärkfors, L., Ebendal, T., Ericsson, A., Holets, V.R. & Persson, H. 1987. Increased  $\beta$ -nerve growth factor messenger RNA and protein in neonatal rat hippocampus following specific cholinergic lesions. *J. Neurosci.* 7: 244-251.
- 101 Carri, N.G. & Ebendal, T. 1987. Target-field specificity in the induction of retinal neurite outgrowth. *Dev. Brain Res.* 31: 83-90.
- 102 Lärkfors, L. & Ebendal, T. 1987. Highly sensitive immunoassays for  $\beta$ -nerve growth factor. *J. Immunol. Meth.* 97: 41-47.
- 103 Ebendal, T., Larhammar, D. & Persson, H. 1986. Structure and expression of the chicken  $\beta$ -nerve growth factor gene. *EMBO J.* 5: 1483-1487.
- 104 Dimberg, Y. & Ebendal, T. 1987. Effects of nerve growth factor on autonomic neurons in the chick embryo. A stereological study. *Int. J. Devl. Neurosci.* 5: 195-205.

- 105 Lärkfors, L., Strömberg, I., Ebendal, T. & Olson, L. 1987. Nerve growth factor protein level increases in the adult rat hippocampus after a specific cholinergic lesion. *J. Neurosci. Res.* 18: 525-531.
- 106 Olson, L., Ayer-LeLievre, C., Ebendal, T. & Seiger, Å. 1987. Nerve growth factor-like immunoreactivities in rodent salivary glands and testis. *Cell Tissue Res.* 248: 275-286.
- 107 Olson, L., Ayer-LeLievre, C., Ebendal, T. & Seiger, Å. 1987. NGF-like immunoreactivities in rodent salivary glands and testis. *Cell Tissue Res.* 248: 275-286.
- 108 Dimberg, Y., Hedlund, K.-O. & Ebendal, T. 1987. Effects of  $\beta$ -nerve growth factor on sensory neurons in the chicken embryo. A stereological study. *Int. J. Devl. Neurosci.* 5: 207-213.
- 109 Ebendal, T. 1987. Comparative screening for ciliary neurotrophic activity in organs of the rat and chicken. *J. Neurosci. Res.* 17: 19-24.
- 110 Ebendal, T., Askmark, H. & Aquilonius, S.-M. 1989. Screening for neurotrophic disturbances in amyotrophic lateral sclerosis. *Acta Neurol. Scand.* 79: 188-193.
- 114 Aquilonius, S.-M., Askmark, H., Ebendal, T. & Gillberg, P.-G. 1987. Neuropharmacology of motor neuron disease. In: *Cellular and Molecular Basis of Cholinergic Function*. (ed. M. J. Dawdal and Hawthorne, J. N.), pp. 729-735. Wiley, Chichester.
- 116 Lärkfors, L., Ebendal, T., Whittemore, S.R., Persson, H., Hoffer, B. & Olson, L. 1987. Decreased level of nerve growth factor (NGF) and its messenger in the aged rat brain. *Mol. Brain Res.* 3: 55-60.
- 117 Ayer-LeLievre, C., Olson, L., Ebendal, T., Seiger, Å. & Persson, H. 1988. Expression of the  $\beta$ -nerve growth factor gene in hippocampal neurons producing NGF mRNA in the brain by *in situ* hybridization. *Science* 240: 1339-1341.
- 119 Hallböök, F., Ebendal, T., & Persson, H. 1988. Production and characterization of biologically active recombinant beta nerve growth factor. *Mol. Cell. Biol.* 8: 452-456.
- 120 Ayer-LeLievre, C., Olson, L., Ebendal, T., Hallböök, F. & Persson, H. 1988. Nerve growth factor mRNA and protein in the testis and epididymis of mouse and rat. *Proc. Natl. Acad. Sci. USA* 85: 2628-2632.
- 121 Carri, N.G., Perris, R., Johansson, S. & Ebendal, T. 1988. Differential outgrowth of retinal neurites on purified extracellular matrix molecules. *J. Neurosci. Res.* 19: 428-439.
- 122 Ebendal, T. & Persson, H. 1988. Detection of nerve growth factor mRNA in the developing chicken embryo. *Development* 102: 101-106.
- 123 Ebendal, T. & Persson, H. 1988. Developmental expression of nerve growth factor. In: *Neural Development and Regeneration* (ed. A. Gorio et al.). NATO ASI Series, Vol. H 22: 233-244. Springer, Berlin.
- 124 Whittemore, Scott R., Persson, H., Ebendal, T., Lärkfors, L., Larhammar, D. &

- Ericsson, A. 1988. Structure and expression of  $\beta$ -nerve growth factor in the rat central nervous system. In: Neural Development and Regeneration (ed. A. Gorio et al.). NATO ASI Series, Vol. H 22: 245-256. Springer, Berlin.
- 125 Strömberg, I., Hultgård-Nilsson, A., Hedin, U. & Ebendal, T. 1988. Fate of intraocular chromaffin cell suspensions: role of initial nerve growth factor support. *Cell Tissue Res.* 254: 487-497.
  - 142 Dimberg, Y. & Ebendal, T. 1988. Effects on injecting antibodies to mouse nerve growth factor into the chick embryo. *Int. J. Devl. Neurosci.* 6: 513-523.
  - 143 Ernfors, P., Hallböök, F., Ebendal, T., Shooter, E.M., Radeke, M.J., Misko, T.P. & Persson, H. 1988. Developmental and regional expression of  $\beta$ -nerve growth factor receptor mRNA in the chick and rat. *Neuron* 1: 983-996.
  - 147 Ayer-LeLievre, C., Ebendal, T., Olson, L., Seiger, Å. & Persson, H. 1989. Detection of nerve growth factor and its mRNA by separate and combined immunohistochemistry and *in situ* hybridization in mouse salivary glands. *Histochem. J.* 21: 1-7.
  - 148 Lärkfors, L., Ebendal, T., Whittemore, S.R., Persson, H., Hoffer, B. & Olson, L. 1988. Developmental appearance of nerve growth factor in the rat brain: significant deficits in the aged forebrain. In: Transplantation into the Mammalian CNS (ed. D.M. Gash & J. R. Sladek, Jr.), *Progr. Brain Res.* 78: 27-31. Elsevier, Amsterdam.
  - 149 Ebendal, T., Persson, H., Larhammar, D., Lundströmer, K. & Olson, L. 1989. Characterization of antibodies to synthetic nerve growth factor (NGF) and proNGF peptides. *J. Neurosci. Res.* 22: 223-240.
  - 150 Nylén, P., Ebendal, T., Eriksson-Nilsson, M., Hansson, T., Henschen, A., Johnson, A.-C., Kronevi, T., Kvist, U., Sjöstrand, N.O., Höglund, G. & Olson, L. 1989. Testicular atrophy and loss of nerve growth factor-immunoreactive germ cell line in rats exposed to n-hexane and a protective effect of simultaneous exposure to toluene or xylene. *Arch. Toxicol.* 63: 296-307.
  - 152 Eriksson-Nilsson, M., Skirboll, S., Ebendal, T., Hersch, L., Grassi, J., Massoulié, J. & Olson, L. 1989. NGF treatment promotes development of basal forebrain tissue grafts in the anterior chamber of the eye. *Exp. Brain Res.* 74: 89-98.
  - 153 Eriksson-Nilsson, M., Skirboll, S., Ebendal, T. & Olson, L. 1989. Nerve growth factor can influence growth of cortex cerebri and hippocampus: Evidence from intraocular grafts. *Neuroscience* 30: 755-766.
  - 154 Strömberg, I. & Ebendal, T. 1989. Aged adrenal medullary tissue survives intraocular grafting, forms nerve fibers and responds to nerve growth factor. *J. Neurosci. Res.* 23: 162-171.
  - 155 Ebendal, T. 1989. Use of collagen gels to bioassay nerve growth factor activity. In: Nerve growth factors (ed. R. A. Rush). *IBRO Handbook series: Methods in the Neurosciences* Vol. 12: 81-93. John Wiley, Chichester.

- 157 Hallböök, F., Persson, H., Barbany, G. & Ebendal, T. 1989. Developmental and regional expression of chicken neuroleukin (glucose-6-phosphate isomerase) messenger RNA. *J. Neurosci. Res.* 23: 142-151.
- 158 Olson, L., Ayer-Le Lievre, C., Bygdeman, M., Ebendal, T., Ernfors, P., Eriksdotter-Nilsson, M., Giacobini, M.B., Henschen, A., Hoffer, B., Mouton, P., Palmer, M., Persson, H., Sara, V., Seiger, Å., Strömberg, I. & Trok, K. 1989. Brain tissue transplantation and growth factors: Basic research and clinical applications. In: *Bioinformatics. Information, Transduction and Processing Systems from Cell to Whole Body* (O. Hatase and J. H. Wang, eds.), pp. 297-304, Elsevier, Amsterdam.
- 159 Carri, N.G. & Ebendal, T. 1989. Staining of developing neurites with Coomassie blue. *Stain Tech.* 64: 50-52.
- 160 Olson, L., Ayer-Lievre, C., Ebendal, T., Eriksdotter-Nilsson, M., Ernfors, P., Mouton, P., Persson, H. & Strömberg, I. 1989. NGF in CNS: Sites of synthesis and effects of novel ways to administer NGF on intrinsic cholinergic neurons and grafts of cholinergic neurons and their target areas. In: *Neuronal Grafting and Alzheimer's Disease* (F. Gage, A. Privat and Y. Christens, eds.), pp. 73-84. Springer, Berlin.
- 161 Ernfors, P., Ebendal, T., Olson, L., Mouton, P., Strömberg, I. & Persson, H. 1989. A cell line producing recombinant nerve growth factor evokes growth responses in intrinsic and grafted central cholinergic neurons. *Proc. Natl. Acad. Sci. USA.* 86: 4756-4760.
- 170 Ebendal, T. 1989. NGF in CNS: Experimental data and clinical implications. *Progr. Growth Factor Res.* 1: 143-159.
- 171 Ebendal, T. 1990. Developmental control of nerve growth factor expression in the nervous system. In: *Regulation of Gene Expression in the Nervous System* (A.-M. Giuffrida-Stella, J. de Vellis and J. Regino Perez-Polo, eds.), *Neurology and Neurobiology*, Vol. 59, pp. 19-30, Wiley-Liss, New York.
- 172 Persson, H., Ernfors, P., Friedman, W., Hallböök, F., Ayer-LeLievre, C., Ebendal, T., Olson, L., Henschen, A., Mouton, P. & Strömberg, I. 1990. Expression of  $\beta$ -nerve growth factor and its receptor in the mammalian central nervous system. In: *Brain Repair* (ed. A. Björklund, A.J. Aguayo and D. Ottoson). *Wenner-Gren Intern. Symp. Series Vol. 56*, pp. 73-86. MacMillan Press, London.
- 173 Ebendal, T., Hallböök, F., Ibáñez, C., Persson, H. & Lärkfors, L. 1990. Activity and immunological properties of recombinant nerve growth factor ( $\beta$ -NGF). In: *Brain Repair* (A. Björklund, A. J. Aguayo and D. Ottoson, eds.), *Wenner-Gren Intern. Symp. Series Vol. 56*, pp. 57-71. MacMillan Press, London.
- 175 Olson, L., Ayer-LeLievre, C., Ebendal, T., Eriksdotter-Nilsson, M., Ernfors, P., Henschen, A., Hoffer, B., Giacobini, M., Mouton, P., Palmer, M., Persson, H., Sara, V., Strömberg, I. & Wetmore, C. 1990. Grafts, growth factors, and grafts that make growth factors. In: *Neural Transplantation: From Molecular Bases to Clinical Application*. *Progr. Brain Res.* 82: 55-65.
- 176 Strömberg, I., Ebendal, T., Olson, L. & Hoffer, B. 1990. Chromaffin grafts:

Survival and nerve fiber formation as a function of donor age, nerve growth factor and host sympathetic denervation. *Progr. Brain Res.* 82: 87-93.

- 177 Friedman, W., Lärkfors, L., Ayer-LeLievre, C., Ebendal, T., Olson, L. and Persson, H. 1990. Regulation of  $\beta$ -nerve growth factor expression by inflammatory mediators in hippocampal cultures. *J. Neurosci. Res.* 27: 374-382.
- 179 Strömberg, I., Wetmore, C.J., Ebendal, T., Ernfors, P., Persson, H. & Olson, L. 1990. Rescue of basal forebrain cholinergic neurons after implantation of genetically modified cells producing recombinant NGF. *J. Neurosci. Res.* 25: 405-411.
- 180 Strömberg, I., Ebendal, T., Eriksdotter-Nilsson, M., Ernfors, P., Friedman, W., Persson, H., Wetmore, C. & Olson, L. 1990. Strategies to increase NGF levels and effect thereof on lesioned and grafted brain tissue. In: *Brain Repair* (A. Björklund, A.J. Aguayo and D. Ottoson, eds.). *Wenner-Gren Intern. Symp. Series Vol. 56*, pp. 87-98, Mac Millan Press, London.
- 181 Mohammed, A. K., Winblad, B., Ebendal, T. & Lärkfors, L. 1990. Environmental influence on behaviour and nerve growth factor in the brain. *Brain Res.* 528: 62-72.
- 185 Hallböök, F., Ayer-LeLievre, C., Ebendal, T. & Persson, H. 1990. Expression of nerve growth factor receptor mRNA during early development of the chicken embryo - emphasis on cranial ganglia. *Development* 108: 693-704.
- 187 Ibáñez, C.F., Hallböök, F., Ebendal, T. & Persson, H. 1990. Structure-function studies of nerve growth factor: Functional importance of highly conserved amino acid residues. *EMBO J.* 9: 1477-1483.
- 191 Ernfors, P., Ibáñez, C. F., Ebendal, T., Olson, L. & Persson, H. 1990. Molecular cloning and neurotrophic activities of a protein with structural similarities to nerve growth factor: Developmental and topographical expression in the brain. *Proc. Natl. Acad. Sci. USA*, 87: 5454-5458.
- 192 Olson, L., Eriksdotter-Nilsson, M., Ernfors, P., Henschen, A., Strömberg, I., Wetmore, C., Ebendal, T. & Persson, H. 1990. On the roles of neurotrophic factors in the CNS: Focus on the NGF/BDNF family. Third Conference, Institute of Developmental Neuroscience and Aging: "Plasticity and regeneration of the nervous system". (Abstr.).
- 193 Aquilonius, S-M., Askmark, H. Ebendal, T. & Gillberg, P.-G. 1992. No re-expression of high-affinity nerve growth factor binding sites in spinal motor neurons in amyotrophic lateral sclerosis. *Eur. Neurol.* 32: 216-218.
- 195 Westermark, K., Nilsson, M., Ebendal, T. & Westermark, B. 1991. Thyrocyte migration and histiotypic follicle regeneration are promoted by EGF in primary culture of thyroid follicles in collagen gel. *Endocrinology* 129: 2180-2186.
- 197 Olson, L., Ayer-LeLievre, C., Björklund, H., Ebendal, T., Hedlund, K.-O., Strömberg, I., Björklund, H., Hökfelt, T., Melander, T., Seiger, Å. & Strömberg, I. 1988. The innervation apparatus of the rodent iris. In: *Handbook of Chemical Neuroanatomy, Vol. 6 The Peripheral Nervous System*, pp. 545-597 (A. Björklund, T. Hökfelt and C. Owman, eds.).



Elsevier.

- 198 Olson, L., Henschen, A., Eriksson-Nilsson, M., Strömberg, I., Wetmore, C., Ernfors, P., Friedman, W., Persson, H. & Ebendal, T. 1990. The expanding role of nerve growth factor in the nervous system. In: *Growth Factors: From Genes to Clinical Application* (Vicki R. Sara et al. eds.) Raven Press, New York, pp. 167-177.
- 199 Söderström, S., Hallböök, C.F., Ibáñez, C.F., Persson, H. & Ebendal, T. 1990. Recombinant human  $\beta$ -nerve growth factor (NGF): Biological activity and properties in an enzyme immunoassay. *J. Neurosci. Res.* 27: 665-677.
- 201 Olson, L., Backlund, E.-O., Ebendal, T., Freedman, R., Hamberger, B., Hansson, P., Hoffer, B., Lindblom, U., Meyerson, B., Strömberg, I., Sydow, O. & Seiger, Å. 1991. Intraputamenal infusion of nerve growth factor to support adrenal medullary autografts in Parkinson's disease: One-year follow-up of first clinical trial. *Arch. Neurol.* 48: 373-381.
- 202 Ibáñez, C. F., Hallböök, F., Söderström, S., Ebendal, T. & Persson, H. 1991. Biological and immunological properties of recombinant human, rat and chicken nerve growth factors: a comparative study. *J. Neurochem.* 57: 1033-1041.
- 203 Lärkfors, L., Oskarsson, A., Sundberg, J. & Ebendal, T. 1991. Methylmercury induced alterations in the nerve growth factor level in the developing brain. *Dev. Brain Res.* 62: 287-291.
- j  
208 Ebendal, T., Söderström, S., Hallböök, F., Ernfors, P., Ibáñez, C.F., Persson, H., Wetmore, C., Strömberg, I. & Olson, L. 1991. Human nerve growth factor: Biological and immunological activities, and clinical possibilities in neurodegenerative disease. In: *Plasticity and Regeneration of the Nervous System* (P. S. Timiras, A. Privat, E. Giacobini, J. Lauder and A. Vernadakis, eds.), *Adv. Exp. Med. Biol.* 296, pp. 207-225. Plenum Publ., N.Y.
- 212 Ibáñez, C.F., Ebendal, T. & Persson, H. 1991. Chimeric molecules with multiple neurotrophic activities reveal structural elements determining the specificities of NGF and BDNF. *EMBO J.* 10: 2105-2110.
- 213 Olson, L., Nordberg, A., von Holst, H., Bäckman, L., Ebendal, T., Alafuzoff, I., Amberla, K., Hartvig, P., Herlitz, A., Lilja, A., Lundqvist, H., Långström, B., Meyerson, B., Persson, A., Viitanen, M., Winblad, B. & Seiger, Å. 1992. Nerve growth factor affects  $^{11}\text{C}$ -nicotine binding, blood flow, EEG, and verbal episodic memory in an Alzheimer patient (Case Report). *J. Neural Transm. (P-D Sect.)* 4: 79-95.
- 214 Hallböök, F., Ibáñez, C. F., Ebendal, T. & Persson, H. 1993. Cellular localization of brain-derived neurotrophic factor and neurotrophin-3 mRNA expression in the early chicken embryo. *Eur. J. Neurosci.* 5: 1-14.
- 215 Olson, L., Wetmore, C., Strömberg, I. & Ebendal, T. 1991. Endogenous and exogenous nerve growth factor in the central nervous system. In: *Volume Transmission in the Brain: Novel Mechanisms for Neural Transmission* (K. Fuxe and L. F. Agnati, eds.), pp. 455-462. Raven Press, Ltd., New York.
- 216 Dimberg, Y., Tottmar, O., Aspberg, A., Ebendal, T., Johansson, K.-J. &

- Walinder, G. 1992. Effects of low-dose X-irradiation on mouse-brain aggregation cultures. *Int. J. Radiat. Biol.* 61: 355-363.
- 217 Ebendal, T., Persson, H. & Olson, L. 1991. New directions in NGF experimental therapy of Alzheimer's disease. In: *Cholinergic Basis for Alzheimer Therapy* (R. Becker and E. Giacobini, eds.), pp. 468-473. Birkhäuser, Boston.
  - 222 Parvinen, M., Pelto-Hoikko, M., Söder, O., Schultz, R., Kaipia, A., Mali, P., Toppari, J., Lönnerberg, P., Ritzen, E. M., Ebendal, T., Olson, L., Hökfelt, T. & Persson, H. 1992. Expression of  $\beta$ -nerve growth factor and its receptor in rat seminiferous epithelium - specific function at the onset of meiosis. *J. Cell Biol.* 117: 629-641.
  - 223 Vazquez, E. M. & Ebendal, T. 1991. Messenger RNAs for *trk* and the low-affinity NGF receptor in rat basal forebrain. *NeuroReport* 2: 593-596.
  - 224 Ibáñez, C. F., Ebendal, T., Barbany, G., Murray-Rust, J., Blundell, T. L. & Persson, H. 1992. Disruption of the low-affinity receptor-binding site in nerve growth factor allows neuronal survival and differentiation by binding to the *trk* gene product. *Cell* 69: 329-341.
  - 225 Carri, N. G., Rubin, K., Gullberg, D. & Ebendal, T. 1992. Neuritogenesis on collagen substrates. Involvement of integrin-like matrix receptors in retinal fibre outgrowth on collagen. *Int. J. Dev. Neurosci.* 10: 393-405.
  - 227 Ekblom, J., Ebendal, T., Gillberg, P.-G., Nordhage, I. & Aquilonius, S.-M. 1992. Quantitative autoradiography of high-affinity nerve growth factor receptors in various segments of the human spinal cord fails to demonstrate alterations in amyotrophic lateral sclerosis. *Neurodegeneration* 1: 163-168.
  - 228 Henriksson, B. G., Söderström, S., Gower, A. J., Ebendal, T., Winblad, B. & Mohammed, A. H. 1992. Hippocampal nerve growth factor levels are related to spatial learning ability in aged rats. *Behav. Brain Res.* 48: 15-20.
  - 229 Persson, H., Ernfors, P., Ibáñez, C. F., Hallböök, F., Friedman, W. J., Merlio, J.-P., Lindvall, O., Bengzon, J., Lindefors, N., Ebendal, T. & Olson, L. 1992. Neurotrophins and their receptors. In: *"Gene Transfer and Therapy in the Nervous System"*. (Fondation Ipsen Meeting). (Eds. F. Gage and W. Cristen), pp 180-200. Springer Verlag, Berlin-Heidelberg.
  - 230 Ebendal, T. 1992. Function and evolution of the NGF family and its receptors. *J. Neurosci. Res.* 32: 461-470.
  - 231 Lorigados, L., Söderström, S. & Ebendal, T. 1992. Two-site enzyme immunoassay for bNGF applied to human patient sera. *J. Neurosci. Res.* 32: 329-339.
  - 232 Carri, N. G., Richardson, P. M. & Ebendal, T. 1994. Choroid coat extract and ciliary neurotrophic factor strongly promote neurite outgrowth in the embryonic chick retina. *Int. J. Dev. Neurosci.* 12: 567-578.
  - 235 Söderström, S. & Ebendal, T. 1995. *In vitro* toxicity of methyl mercury: effects on nerve growth factor (NGF)-responsive neurons and on NGF synthesis in fibroblasts. *Toxicol. Lett.* 75: 133-144.
  - 236 Palmer, M. R., Eriksdotter-Nilsson, M., Henschen, A., Ebendal, T. & Olson, L.

1993. Nerve growth factor-induced excitation of selected neurons in the brain which is blocked by a low-affinity receptor antibody. *Exp. Brain Res.* 93: 226-230.
- 237 Söderström, S., Fredriksson, A., Dencker, L. & Ebendal, T. 1995. The effect of mercury vapour on cholinergic neurons in the fetal brain: studies on the expression of nerve growth factor and its high- and low-affinity receptors. *Dev. Brain Res.* 85: 96-108.
  - 239 Bengzon, J., Söderström, S., Kokaia, Z., Kokaia, M., Ernfors, P., Persson, H., Ebendal, T. & Lindvall, O. 1992. Widespread increase of nerve growth factor protein in the rat forebrain after kindling-induced seizures. *Brain Res.* 587: 338-342.
  - 241 Williams, R., Bäckström, A., Ebendal, T. & Hallböök, F. 1993. Molecular cloning and cellular localization of *trkC* in the chicken embryo. *Dev. Brain Res.* 75: 235-252.
  - 242 Williams, R., Bäckström, A., Kullander, K., Hallböök, F. & Ebendal, T. 1995. Developmentally-regulated expression of mRNA for neurotrophin high-affinity (*trk*) receptors within chick trigeminal sensory neurons. *Eur. J. Neurosci.* 7: 116-128.
  - 243 Kullander, K. & Ebendal, T. 1994. Neurotrophin-3 acquires NGF-like activity after exchange to five NGF amino acid residues: Molecular analysis of the sites in NGF mediating the specific interaction with the NGF high affinity receptor. *J. Neurosci. Res.* 39: 195-210.
  - 244 Durbeej, M., Söderström, S., Ebendal, T. & Ekblom, P. 1993. Differential expression of neurotrophin receptors during renal development. *Development* 119: 977-989.
  - 249 Granholm, A.-C., Bäckman, C., Bloom, F., Ebendal, T., Gerhardt, G., Hoffer, B., Mackerlova, L., Olson, L., Söderström, S., Walus, L. R. & Friden, P. M. 1994. NGF and anti-transferrin receptor antibody conjugate - Short and long-term effects on survival of cholinergic neurons in intraocular septal transplants. *J. Pharmacol. Exp. Ther.* 268: 448-459.
  - 250 Jazin, E. E., Zhang, X., Söderström, S., Williams, R., Hökfelt, T., Ebendal, T. & Larhammar, D. 1993. Expression of peptide YY and mRNA for the NPY/PYY receptor of the Y1 subtype in dorsal root ganglia during rat embryogenesis. *Dev. Brain Res.* 76:105-113.
  - 251 Schwarting, R.K.W., Pei, G., Söderström, S., Ebendal, T. & Huston, J.P. 1994. Unilateral stimulation or removal of rat vibrissae: analysis of nerve growth factor and tyrosine hydroxylase mRNA in the brain. *Behav. Brain Res.* 60: 63-71.
  - 252 Humpel, C., Ebendal, T., Cao, Y., & Olson, L. 1993. Pentylentetrazol seizures increase pro-nerve growth factor-like immunoreactivity in the reticular thalamic nucleus and nerve growth factor mRNA in the dentate gyrus. *J. Neurosci. Res.* 35: 419-427.
  - 253 Ekblom, J., Jossan, S. S., Ebendal, T., Söderström, T., Orelund, L. & Aquilonius, S.-M. 1994. mRNA expression of neurotrophins and members of the *trk* family in the rat brain after treatment with L-deprenyl. *Acta Neurol. Scand.* 89: 147-148.
  - 255 Granholm, A.-C., Biddle, P. T., Bäckman, C., Ebendal, T., Gerhardt, G., Hoffer, B., Mackerlova, L., Olson, L., Söderström, S., Walus, L. & Friden, P. 1994. Peripheral administration of nerve growth factor conjugated to an anti-transferrin receptor antibody increases cholinergic neuron survival in intraocular forebrain transplants. In "Methods in Neurosciences". Providing pharmacological access to the brain: Alternate

approaches. Vol. 21 (T.R. Flanagan, D.F. Emerich and S. Vinn, Eds.), pp. 71-92.  
Academic Press, N.Y.

- ) 256 Seiger, Å., Nordberg, A., von Holst, H., Bäckman, L., Ebendal, T., Alafuzoff, I., Amberla, K., Hartvig, P., Herlitz, A., Lilja, A., Lundqvist, H., Långström, B., Meyerson, B., Persson, A., Viitanen, M., Winblad, B. & Olson, L. 1993. Intracranial infusion of purified nerve growth factor to an Alzheimer patient: The first attempt of possible future treatment strategy. In: Alzheimer's Disease: Animal Models and Clinical Perspectives. (A. Mohammed, B. Henriksson, B. Winblad and P. Södersten, Eds.), Behav. Brain Res. 57: 255-261.
- 265 Bartheld, C. S. von, Schober, A., Kinoshita, Y., Williams, R., Ebendal, T. & Bothwell, M. 1995. Noradrenergic neurons in the locus coeruleus of birds express TrkA, transport NGF and respond to NGF. J. Neurosci. 15: 2225-2239.
- 266 Lorigados, L., Molina, H., Serrano, T., Pavón, N., Robinson, M.A., Alvarez, L., Söderström, S. & Ebendal, T. 1995. Evolutive levels of NGF in neurodegenerative disorders. Mol. Chem. Neuropathol. 24: 231-234.
- 269 Ebendal, T., Tomac, A., Hoffer, B. J. & Olson, L. 1995. Glial cell line-derived neurotrophic factor (GDNF) stimulates fibre formation and survival in cultured neurons from peripheral autonomic ganglia. J. Neurosci. Res. 40: 276-284.
- 276 Hallböök, F., Bäckström, A., Kullander, K., Ebendal, T. & Carri, N. 1996. Expression of neurotrophins and trk receptors in the avian retina. J. Comp. Neurol. 364: 664-676.
- ) 277 Humpel, C., Lindqvist, E., Söderström, S., Kylberg, A., Ebendal, T. & Olson, L. 1995. Monitoring release of neurotrophic activity in the brains of awake rats. Science 269: 552-554.
- 278 Bäckman, C., Biddle, P. T., Ebendal, T., Friden, P., Gerhardt, G., Henry, M., Mackerlova, L., Söderström, S., Strömberg, I., Walus, L., Hoffer, B. J. & Granholm, A.-Ch. 1995. Effects of transferrin receptor antibody-NGF conjugate on young and aged septal transplants *in oculo*. Exp. Neurol. 132: 1-15.
- 279 Pei, G. & Ebendal, T. 1995. Specific lesions in the extrapyramidal system of the rat brain induced by 3-nitropropionic acid (3-NPA). Exp. Neurol. 132: 105-115.
- 280 Hallböök, F., Bäckström, A., Kullander, K., Kylberg, A., Williams, R. & Ebendal, T. 1995. Neurotrophins and their receptors in chicken neuronal development. Int. J. Dev. Biol. 39: 855-868.
- 281 Holst, A. von, Rodriguez-Tébar, A., Michaille, J.J., Dhouailly, D., Bäckström, A., Ebendal, T. & Rohrer, H. 1995. Retinoic acid-mediated increase in *TrkA* expression is sufficient to elicit NGF-dependent survival of sympathetic neurons. Mol. Cell. Neurosci. 6: 185-198.
- ) 282 Sydow, O., Hansson, P., Young, D., Meyerson, B., Backlund, E.-O., Ebendal, T., Farnebo, L. O., Freedman, R., Hamberger, B., Hoffer, B., Seiger, Å., Strömberg, I., & Olson, L. 1995. Long-term beneficial effects of adrenal medullary autografts supported by nerve growth factor in Parkinson's

disease. Eur. J. Neurol. 2: 445-454.

- 283 Tomac, A., Widenfalk, J., Lin, L-F. H., Kohno, T., Ebendal, T., Hoffer, B. J. & Olson, L. 1995. Retrograde axonal transport of glial cell line-derived neurotrophic factor in the adult nigrostriatal system suggests a trophic role in the adult. Proc. Natl. Acad. Sci. USA 92: 8274-8278.
- 285 Söderström, S. & Ebendal, S. 1995. Levels of neurotrophin-3 protein in the rat brain as determined by enzyme immunoassay show a pattern distinct from nerve growth factor. Neurosci. Lett. 189: 5-8.
- 286 Hallböök, F., Ebendal, T. & Carri, N.G. 1995. Neurotrophins in the developing avian visual system. In: "Life and Death in the Nervous System. Role of Neurotrophic Factors and their Receptors". Wenner-Gren Foundation International Series Vol. 67 (C. Ibáñez, T. Hökfelt, L. Olson, K. Fuxe, H. Jörnvall and D. Ottoson, Eds.), pp. 143 - 153. Stockholm, Sweden.
- 287 Williams, R., Bäckström, A. & Ebendal, T. 1995. Embryonic expression of neurotrophin high-affinity (*trk*) receptor mRNAs within sensory neurons: chicken development as a model. In: "Life and Death in the Nervous System. Role of Neurotrophic Factors and their Receptors". Wenner-Gren Foundation International Series Vol. 67 (C. Ibáñez, T. Hökfelt, L. Olson, K. Fuxe, H. Jörnvall and D. Ottoson, Eds), pp. 113 - 130. Stockholm, Sweden.
- 290 Martínez-Serrano, A., Fischer, W., Söderström, S., Ebendal, T. & Björklund, A. 1996. Long-term functional recovery from age-induced spatial memory impairments by nerve growth factor gene transfer to the rat basal forebrain. Proc. Natl. Acad. Sci. USA 93: 6355-6360.
- 291 Durbeej, M., Fecker, L., Hjalt, T., Zhang, H.-Y., Salmivirta, K., Klein, G., Timpl, R., Sorokin, L., Ebendal, T., Ekblom, P. & Ekblom, M. 1996. Expression of laminin  $\alpha 1$ ,  $\alpha 5$  and  $\beta 2$  chains during embryogenesis of the kidney and vasculature. Matrix Biol. 15: 397-413.
- 292 Hasenöhrl, R.U., Söderström, S., Mohammed, A.H., Ebendal, T. & Huston, J.P. 1997. Reciprocal changes in expression of mRNA for nerve growth factor and its receptors TrkA and LNGFR in brain of aged rats in relation to maze learning deficits. Exp. Brain Res. 114: 205-213.
- 293 Bengtsson, H., Söderström, S. & Ebendal, T. 1995. Expression of activin receptors type I and II only partially overlaps in the nervous system. NeuroReport 7: 113-116.
- 294 Estenne-Bouhtou, G., Kullander, K., Karlsson, M., Ebendal, T., Hacksell, U., & Luthman, K. 1996. Design, synthesis, tandem mass spectrometric sequencing, and biological activity of NGF-mimetics. Int. J. Peptide Prot. Res. 48: 337-346.
- 296 Williams, R. & Ebendal, T. 1995. Neurotrophin receptor expression during development of the chick spinal sensory ganglion. NeuroReport 6: 2277-2282.
- 300 McGrath, J.P., Cao, X., Schutz, A., Lynch, A., Ebendal, T., Coloma, M.J., Morrison, S.L. & Putney, S.D. 1997. Bifunctional fusion between nerve growth factor and a transferrin receptor antibody. J. Neurosci. Res. 47: 123-133.
- 301 Nosrat, C.A., Ebendal, T. & Olson, L., 1996. Differential expression of brain-derived neurotrophic factor and neurotrophin 3 mRNA in lingual papillae and taste buds

indicates roles in gustatory and somatosensory innervation. *J. Comp. Neurol.* 376: 587-602.

- 303 Aoyagi, K., Bergsten, P., Eriksson, U.J., Ebendal, T. & Hellerström, C. 1997. *In vitro* regulation of insulin release and biosynthesis of fetal rat pancreatic cells explanted on pregnancy day 16. *Biol. Neonate* 71: 60-68.
- 305 Kobayashi, S., Ögren, S.-O., Ebendal, T. & Olson, L. 1997. Intraventricular injection of NGF, but not BDNF, induces rapid motor activation that is inhibited by nicotinic receptor antagonists. *Exp. Brain Res.* 116: 315-325.
- 306 Lewén, A., Söderström, S., Hillered, L. & Ebendal, T. 1997. Expression of serine/threonine kinase receptors in traumatic brain. *NeuroReport* 8: 475-479.
- 307 Söderström, S., Bengtsson, H. & Ebendal, T. 1996. Expression of serine-threonine protein kinase receptors including the bone morphogenetic factor type II receptor in developing and adult rat brain. *Cell Tiss. Res.* 286: 269-279.
- 309 Bäckström, A., Söderström, S., Kylberg, A. & Ebendal, T. 1996. Molecular cloning of the chicken *trkA* and its expression in early peripheral ganglia. *J. Neurosci. Res.* 44: 77-81.
- 311 Nosrat, C., Tomac, A., Lindqvist, E., Lindskog, S., Humpel, C., Strömberg, L., Hoffer, B.J. & Olson, L. 1996. Cellular expression of GDNF mRNA suggests multiple functions inside and outside the nervous system. *Cell Tissue Res.* 285: 207.
- 312 Lorentzon, M., Hoffer, B., Ebendal, T., Olson, L. & Tomac, A. 1996. *Habrec1*, a novel serine/threonine kinase TGF $\beta$  type I-like receptor, has a specific cellular expression suggesting function in the developing organism and adult brain. *Exp. Neurol.* 145: 351-360.
- 313 Humpel, C., Ebendal, T. & Olson, L. 1996. Microdialysis: a way to study in vivo of neurotrophic bioactivity: A critical summary. *J. Mol. Med.* 74: 523-526.
- 318 Kullander, K., Kaplan, D. & Ebendal, T. 1997. Two restricted sites on the mature NGF molecule independently determine specific TrkA receptor binding and internalization. *J. Biol. Chem.* 272: 9300-9307.
- 319 Carri, N.G., Bengtsson, H., Charette, M.F. & Ebendal, T. 1998. BMP receptor II expression and OP-1 effects in developing chicken retinal explants. *NeuroReport* 9 (in press).
- 320 Bäckström, A., Söderström, S. & Ebendal, T. 1997. Cloning of a new chicken *trkB* extracellular isoform and its mRNA expression in E9 sensory and autonomic ganglia. *Int. J. Dev. Neurosci.* 15: 275-284.
- 321 Dimberg, Y., Vazquez, E. M., Söderström, S. & Ebendal, T. 1997. Effects of irradiation on nerve growth factor in the developing mouse brain. *Toxicol. Lett.* 90: 35-43.
- 322 Nordberg, A., Almkvist, O., Amberla, K., Basun, H., Corder, B., Ebendal, T., Forsell, C.-G., Hartwig, P., Hellström-Lindahl, E., Jelic, V., Jönhagen, M., Lannfelt, L., Lehman, W., Långström, B., Lundquist, H., Meurling, L., Meyersson, B., Olson, L., Seiger, Å., Valind, S., Viitanen, M., Wahlund, L.-O. & Winblad, B. 1997. Response and non-responders to tacrine, ondansetron and NGF treatment in Alzheimer patients evaluated by positron emission tomography and APOE genotype. In: *Alzheimer's*

- 323 Kobayashi, S., Ögren, S.-O., Ebendal, T. & Olson, L. 1997. Dopamine receptor antagonists block NGF-induced hyperactivity. *Eur. J. Pharmacol.* 326: 1-5.
- 324 Lindeberg, J., Klint, P., Bäckström, A., Williams, R. & Ebendal, T. 1997. Identification of a chicken homologue in the Brn-3 subfamily of POU-transcription factors. *Dev. Brain Res.* 100: 169-182.
- 325 Granholm, A.-C., Albeck, D., Bäckman, C., Curtis, M., Ebendal, T., Friden, P., Henry, M., Hoffer, B., Kordower, J., Rose, G.M., Söderström, S. and Bartus, R.T. 1998. A non-invasive system for delivering neural growth factors across the blood-brain barrier: a review. *Rev. Neurosci.* (in press).
- 326 Kullander, K., Kylberg, A. & Ebendal, T. 1997. Specificity of neurotrophin-3 determined by loss-of-function mutagenesis. *J. Neurosci. Res.* 50: 496-503.
- 327 Jazin, E.E., Söderström, S., Ebendal, T. & Larhammar, D. 1997. Embryonic expression of the mRNA for the rat homologue of the fusin/CXCR-4 HIV-1 co-receptor. *J. Neuroimmunol.* 79: 148-154.
- 329 Riikonen, R., Söderström, S., Vanhala, R., Ebendal, T. & Lindholm, D.B. 1997. West's syndrome: Cerebrospinal fluid nerve growth factor and effect of ACTH. *Pediatr. Neurol.* 17: 224-229.
- 330 Kobayashi, S., Ögren, S.-O., Ebendal, T. & Olson, L. 1997. Intraventricular injection of NGF, but not BDNF, induces rapid motor activation that is inhibited by nicotinic receptor antagonists. *Exp. Brain Res.* 116: 315-325.
- 331 Nosrat, C., Fried, K., Ebendal, T., & Olson, L. 1998. NGF, BDNF, NT3, NT4 and GDNF in tooth development. *Eur. J. Oral. Sci.* 106 (suppl. 1): 94-99.
- 332 Kadari, A., Windisch, J.M., Ebendal, T., Schneider, R. & Humpel, C. 1997. Cell death of adult pyramidal CA1 neurons after intraventricular injection of a novel peptide derived from *trkA*. *J. Neurosci. Res.* 50: 402-412.
- 337 Eriksdotter Jönhagen, M., Amberlaa, K., Bäckman, L., Ebendal, T., Meyerson, B., Nordberg, A., Olson, L., Seiger, Å., Shigeta, M., Theodorson, E., Wahlund, L.-O., Viitanen, M. & Winblad, B. 1998. Intracerebroventricular infusion of nerve growth factor in three patients with Alzheimer's disease. *Dementia Geriatric Cogn. Disord.* (in press).
- 338 Ebendal, T., Bengtsson, H. & Söderström, S. 1998. Bone morphogenetic proteins and their receptors: potential functions in the brain. *J. Neurosci. Res.* 51: 139-146.